Remarks

The claims are 1-12. Claims 1-12 have been amended to correct grammatical mistakes and to better define the claimed invention's 5-membered ring **A**. Support for the changes can be found in the original claims and in the examples. Accordingly, the changes do not constitute new matter.

I. Claim Objections

The dependent claims have been objected to as not starting with the word "The". The dependent claims have been amended to start with that word. The errant period mark after the word "unsubstituted" has been removed. Applicants respectfully submit that the objections have been overcome and request their withdrawal.

II. Rejections Under 35 USC 112

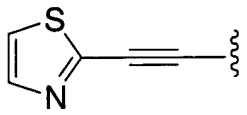
The claims have been rejected as allegedly not described in the specification to enable one in the art to make/use the invention. The Examiner asserts that the disclosure provides little direction to any of the factors of the subject being treated, the formulation of the dosage form, the particular disease state or condition, the therapeutic threshold and the mode of administration. Applicants respectfully submit that the skilled artisan in the pharmaceutical arts well understands the recited factors, particularly in light of the specification's disclosure of the subject being treated described at page 17, lines 8-17; the formulation of the dosage form described at page 18, line 3 to page 20, line 30, including specific dosages recited at page 20, lines 28-30; the particular disease state or condition described at page 17, line 18 to page 18, line 2; the therapeutic threshold described by assays at page 21, lines 13-29, followed by testing procedures routinely and commonly used in the pharmaceutical arts and industry; and the mode of administration described at page 18, lines 3-13.

One of ordinary skill in the pharmaceutical industry and art readily understands how to make and/or use the invention from the above disclosures, utilizing experimentation routinely and commonly performed. The length and amount of experimentation, in and of themselves, do not rise to the level of undue experimentation if the industry and art routinely and commonly perform experiments to such lengths and number. Accordingly, Applicants respectfully submit that the rejections have been overcome and request their withdrawal.

III Rejections Under 35 USC 102 and 103

The claims have been rejected as allegedly anticipated or made obvious by WO 96/33181 ('181 reference). Applicants respectfully submit that the '181 reference does not anticipate or make obvious the claims, as presently amended.

The '181 reference describes ethynylthiazole compounds in which the thiazole and ethynyl moieties are joined at a site adjoining a sulfur heteroatom and a nitrogen heteroatom:



The compounds of the present claims require that at least one of the adjoining atoms be carbon. Thus, the '181 reference does not disclose the compounds of the present application as claimed in independent claims 1, 4, 9, and 11, as amended. Accordingly, Claims 1, 4, 9, and 11 are not anticipated by the '181 reference. Claims 2-3, 5-8, 10 and 12, depending from the independent claims, are also not anticipated by the '181 reference for that reason as well as for the additional limitations they contain.

The '181 reference describes ethynylthiazole compounds in which the thiazole and ethynyl moieties are joined at a site adjoining a sulfur heteroatom and a nitrogen heteroatom that are leukotriene antagonists. The '181 reference does not describe, disclose, suggest, teach, or motivate the compounds of the present application as claimed in independent claims 1, 4, 9, and 11, as amended or their use to mediate excitatory neurotransmitter metabotropic glutamate receptor of the mammalian central nervous system. Accordingly, the '181 reference does not make obvious independent claims 1, 4, 9, and 11, as amended. Claims 2-3, 5-8, 10 and 12, depending from the independent claims, are also not made obvious for that reason as well as for the additional limitations they contain.

Applicants respectfully submit that the rejections have been overcome and request their withdrawal.

Conclusion

Applicants respectfully submit that the application is in condition for allowance and request a Notice to that effect. Attorney for Applicants can be reached at the telephone number and address below. Correspondence should be sent to the new address

below. Any additional fees or deficiency in fees required should be taken from Merck Deposit Account No. **13-2755**.

Respectfully submitted,

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on the date appearing below.

MERCK & CO., INC.

By Shu M. Lee Date 13 June 2001

By Shu M. Lee

Shu M. Lee
Reg. No. 41,147
Attorney for Applicants

MERCK & CO., Inc.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-2675

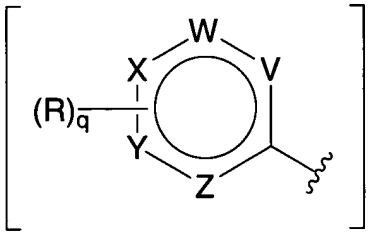
Date: June 13, 2001

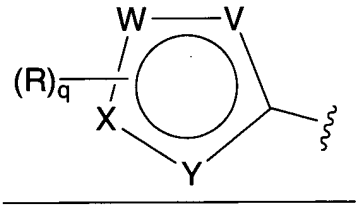
CLAIMS MARKED-UP TO SHOW CHANGES:

Claim 1. (Amended Twice) A method of modulating the activity of excitatory amino acid receptors, said method comprising:

contacting said receptors with at least one compound having the structure **A-L-B** or enantiomers, diastereomeric isomers or mixtures of any two or more thereof, or pharmaceutically acceptable salts thereof, in an amount sufficient to modulate the activity of said excitatory amino acid receptor, wherein:

A is a 5-membered ring having the structure:





wherein at least one of V and Y is CH or CR;

at least one of **V**, **W**, **X**, and **Y** [and **Z**] is $(CR)_p$, wherein p is [0,] 1 [or 2];

at least one of **V**, **W**, **X**, and **Y** [and **Z**] is S;

the remainder of **V**, **W**, **X**, and **Y** [and **Z**] are each N; and

each **R** is independently halogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted[.] aryl, heterocycle, mercapto, nitro, carboxyl, carbamate, carboxamide, hydroxy, ester, cyano, amine, amide, amidine, amido, sulfonyl or sulfonamide, wherein q is 0, 1, or 2;

L is alkynylene; and

B is substituted or unsubstituted aryl.

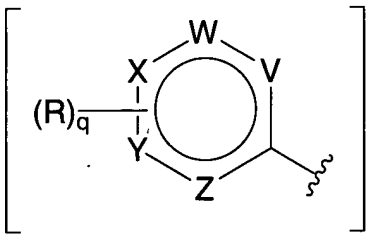
Claim 2. (Amended) [A] The method according to claim 1, wherein said excitatory amino acid receptor is a metabotropic glutamate receptor.

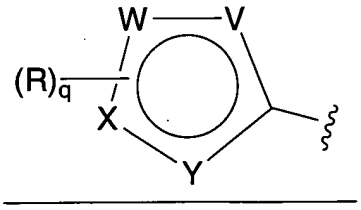
Claim 3. (Amended) [A] The method according to claim 2, wherein said metabotropic glutamate receptor is a Group 1 metabotropic glutamate receptor.

Claim 4. (Amended Twice) A method for treating disease conditions, said method comprising:

administering to a patient having a disease condition a therapeutically effective amount of at least one compound having the structure **A-L-B** or enantiomers, diastereomeric isomers or mixtures of any two or more thereof, or pharmaceutically acceptable salts thereof, wherein:

A is a 5-membered ring having the structure:





wherein at least one of V and Y is CH or CR;

at least one of **V**, **W**, **X**, and **Y** [and **Z**] is $(CR)_p$, wherein p is [0,] 1 [or 2];

at least one of **V**, **W**, **X**, and **Y** [and **Z**] is S;

the remainder of **V**, **W**, **X**, and **Y** [and **Z**] are each N; and

each **R** is independently halogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted aryl, heterocycle, mercapto, nitro, carboxyl, carbamate, carboxamide, hydroxy, ester, cyano, amine, amide, amidine, amido, sulfonyl or sulfonamide, wherein q is 0, 1, or 2;

L is alkynylene; and

B is substituted or unsubstituted aryl.

Claim 5. (Amended) [A] The method according to claim 4, wherein said disease condition is cerebral ischemia, chronic neurodegeneration, psychiatric disorders, schizophrenia, mood disorders, emotion disorders, disorders of extrapyramidal motor function, obesity, disorders of respiration, motor control and function, attention deficit disorders, concentration disorders, pain disorders, neurodegenerative disorders, epilepsy, convulsive disorders, eating disorders, sleep disorders, sexual disorders, circadian disorders, drug withdrawal, drug addiction, compulsive disorders, anxiety, panic disorders, depressive disorders, skin disorders, retinal ischemia, retinal degeneration, glaucoma, disorders associated with organ transplantation, asthma, ischemia or astrocytomas.

Claim 6. (Amended) [A] The method according to claim 5, wherein said mood disorder is anxiety, depression, psychosis, drug withdrawal, tobacco withdrawal, memory loss, cognitive impairment, dementia, or Alzheimer's disease.

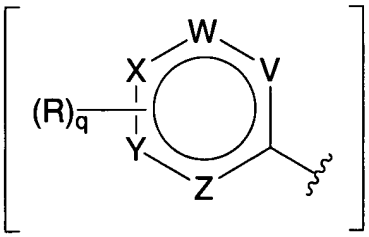
Claim 7. (Amended) [A] The method according to claim 5, wherein said extrapyramidal motor function is Parkinson's disease, progressive supramuscular palsy, Huntington's disease, Gilles de la Tourette syndrome, or tardive dyskinesia.

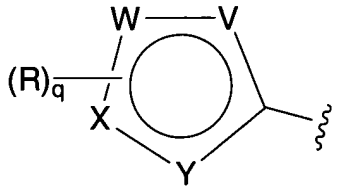
Claim 8. (Amended) [A] The method according to claim 5, wherein said pain disorder is neuropathic pain, chronic pain, acute pain, painful diabetic neuropathy, post-herpetic neuralgia, cancer-associated pain, pain associated with chemotherapy, pain associated with spinal cord injury, pain associated with multiple sclerosis, causalgia and reflex sympathetic dystrophy, phantom pain, post-stroke (central) pain, pain associated with HIV or AIDS, trigeminal neuralgia, lower back pain, myofacial disorders, migraine, osteoarthritic pain, postoperative pain, dental pain, post-bum pain, pain associated with systemic lupus, entrapment neuropathies, painful polyneuropathies, ocular pain, pain associated with inflammation or pain due to tissue injury.

Claim 9. (Amended Twice) A method for preventing disease conditions in a subject at risk thereof, said method comprising:

administering to said subject a therapeutically effective amount of at least one compound having structure **A-L-B** or enantiomers, diastereomeric isomers or mixtures of any two or more thereof, or pharmaceutically acceptable salts thereof, wherein:

A is a 5-membered ring having the structure:





wherein at least one of V and Y is CH or CR;

at least one of **V**, **W**, **X**, and **Y** [and **Z**] is $(CR)_p$, wherein p is [0,] 1 [or 2];

at least one of **V**, **W**, **X**, and **Y** [and **Z**] is S;

the remainder of **V**, **W**, **X**, and **Y** [and **Z**] are each N; and

each **R** is independently halogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted aryl, heterocycle, mercapto, nitro, carboxyl, carbamate, carboxamide, hydroxy, ester, cyano, amine, amide, amidine, amido, sulfonyl or sulfonamide, wherein q is 0, 1, or 2;

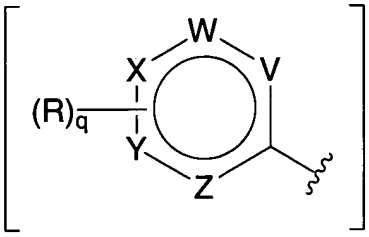
L is alkynylene; and

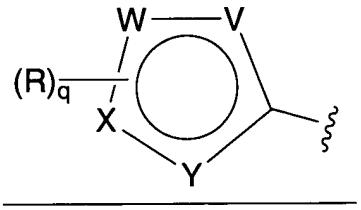
B is substituted or unsubstituted aryl.

Claim 10. (Amended) [A] The method according to claim 9, wherein said disease is a disease of the pulmonary system, a disease of the nervous system, a disease of the cardiovascular system, a disease of the gastrointestinal system, a disease of the endocrine system, a disease of the exocrine system, a disease of the skin, cancer or a disease of the ophthalmic system.

Claim 11. (Amended Twice) A pharmaceutically acceptable salt form of a compound, said compound having the formula **A-L-B** or enantiomers, diastereomeric isomers or mixtures of any two or more thereof, wherein:

A is a 5-membered ring having the structure:





wherein at least one of V and Y is CH or CR;

at least one of **V**, **W**, **X**, and **Y** [and **Z**] is $(CR)_p$, wherein p is [0,] 1 [or 2];

at least one of **V**, **W**, **X**, and **Y** [and **Z**] is S;

the remainder of **V**, **W**, **X**, and **Y** [and **Z**] are each N; and

each **R** is independently halogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted aryl, heterocycle, mercapto, nitro, carboxyl, carbamate, carboxamide, hydroxy, ester, cyano, amine, amide, amidine, amido, sulfonyl or sulfonamide, wherein q is 0, 1, 2 or 3;

L is alkynylene; and

B is substituted or unsubstituted aryl; and

the salt is acetate, adipate, alginate, aspartate, benzoate, benzenesulfonate, butyrate, citrate, camphorate, camphorsulfonate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, glucoheptanoate, glycerophosphate, heptanoate, hexanoate, 2-hydroxyethanesulfonate, lactate, malate, maleate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, oxalate, tartrate, toluenesulfonate, undecanoate, sulfate, bisulfate, hemisulfate, hydrochloride, hydrobromide, hydroiodide, an ammonium salt, an alkali metal salt, an alkaline earth metal salt, a dicyclohexylamine salt, N-methyl-D-glucamine, phenylethylamine, or an amino acid salt.

Claim 12. (Amended) The pharmaceutically acceptable salt form of the compound according to Claim 1, wherein the salt is a toluene sulfonic acid salt.